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Research Article

Pyogenic Spinal Infection: is Expanded Dengue Syndrome A Risk Factor? – A Series of Ten Cases and Brief Literature Review

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Abstract

Background: An acute surge of pyogenic spinal infection was noted during the recent dengue epidemic in Kerala. Review of literature does not show any association between Dengue fever (DF) and pyogenic spinal infections, though immunosuppression is a well-known risk factor. We report ten such cases of spinal infections to create an awareness among the medical fraternity thereby aiding early management.

Methods and Material: A retrospective review of patients with spinal infections and DF during the month of June and July 2017. No statistical analysis was used.

Results: We had ten patients of DF presenting with varying degrees of neurological compromise and a spectrum of spondylitis, spondylodiscitis and epidural abscess. None of them had significant back pain prior to DF. Though various risk factors like diabetes mellitus and intravenous catherization were present, all of them consistently had documented Expanded dengue syndrome (transient leukopenia, neutropenia and culture positive bacteraemia with DF).

Conclusions: We conclude that there appears to be an association between spinal infections and DF with neutropenia. It is highly recommended that it be considered a part of the expanded dengue syndrome for creating awareness among the physicians, thereby preventing any delay in management.

Keywords: *Pyogenic Spinal Infection; Dengue Fever; Neutropenia*

Introduction

Pyogenic cause for spinal infections are relatively uncommon (2 - 7% of musculoskeletal infection). It was first described as pyogenic osteomyelitis in the medical literature by Lannelonge in 1879 [1]. Though neutropenia, immunosuppression and various other risk factors have been documented, no such reports of an association between neutropenia in DF and pyogenic spine infections could be found. Thein TL et al in their study concluded that neutropenia in dengue patients are not predictive of secondary bacterial infections[2]. Based on our observations in this study we would like to hypothesize that spinal infections occur more commonly in expanded dengue syndrome.

Materials and Methods

We conducted a retrospective review of dengue related spinal infections in our centre- an 800-bedded tertiary care hospital, during the months of June and July 2017. This period coincided with the dengue epidemic in Kerala. 1138 patients were diagnosed with DF in our hospital. During this period, we had encountered 12 cases of spinal infections and of them ten patients had associated dengue fever. In an attempt to decode the causation and risk factors, the records of these patients were reviewed in detail with respect to patient details, blood work up, spinal level, causative organism, pre-treatment neurology, treatment and follow up. A brief literature review on spinal infections, dengue with neutropenia using PubMed database was done.

Results

The details of patients with dengue associated spinal infection were tabulated and analysed (Table 1).

Patient	Age	Sex	Comorbidities	Diagnosis	Frankel	Surgery	Organism
1	62	M	T2DM **, SHT§, PCI ††	C6-7 discitis C2-C7 epidural abscess	C	C2-7 laminectomy, decompression + C6-7 ACDF	MRSA *
2	75	F	SHT§	L2-3 Discitis with spondylolisthesis	E	L2-4 posterior instrumentation, laminectomy, debridement and fusion L3-4	P.Aeruginosa
3	54	F	T2DM **, SHT§	D6-L2 epidural abscess	D	D6-L2 Laminectomy and decompression	MRSA *
4	30	M	No	L4-5 discitis with epidural abscess	D	L4 laminectomy and debridement	MRSA *
5	58	M	T2DM **	L4-5, L5-S1 Septic arthritis of facet joint with right psoas abscess	D	L3-S1 posterior instrumentation, laminectomy and decompression. I&D psoas abscess	MSSA †
6	60	F	No	C5-6 discitis and osteomyelitis	D	C5, C6 corpectomy, decompression C4-7 fusion	MRSA *
7	71	M	COPD ‡, BPH‡‡	L4-5 discitis D4 transverse myelitis	C	Medical management	MRSA *
8	75	M	CVA ||, T2DM **	C6-7 discitis with epidural abscess	C	Medical management	MRSA *
9	62	M	No	T12-L1 discitis	E	Debridement and instrumented fusion	MRSA *
10	58	F	T2 DM **	L4-5 discitis with epidural abscess	D	Debridement and instrumented fusion	MRSA *

Table 1: *Summary of ten patients with spinal infections post dengue.*

*- Methicillin resistant staphylococcus aureus, †- Methicillin sensitive staphylococcus aureus, ‡- Chronic obstructive pulmonary disease, §- Systemic hypertension, ||- Cerebral vascular disease, **- Type 2 diabetes mellitus, ††- Percutaneous coronary intervention, ‡‡- Benign prostatic hypertrophy.

The review had six males and four females. Nine patients were above 50 years of age with most of them clustered within 55 to 75 years of age. Five patients had type 2 diabetes mellitus. Five patients had other comorbidities in the form of hypertension, obstructive lung disease or stroke. The average duration between the diagnosis of DF and spinal infection was 14 days ranging from eight days to one month. Seven patients were readmitted for neurological symptoms after getting discharged following DF.

Vertebral segment distribution pattern included three cervical spine, one dorsal spine, one dorso-lumbar junction and seven lumbar spines. One patient had involvement of both dorsal and lumbar spine. Most common levels encountered were C6-7and L4 - 5. All these patients had history of seropositive dengue confirmed by either NS-1 antigen, ELISA or both.

A thorough analysis of their labs revealed that all of them had a period of transient leukopenia (Total leucocyte count < 4 x 10^3 per cm) with an average of 2.53 x 10^3 cells/cm. Coinciding with leukopenia four patients had moderate neutropenia (Absolute Neutrophil Count (ANC)= 500-1000), Four patients had mild neutropenia (ANC 1000-1500), and two patients had borderline neutropenia (ANC > 1500).

We had observed a constant trend in the leucocyte count of these patients. The period of transient leukopenia clustered around the 4^{th} and 5^{th} day of onset of fever. Leucocyte count gradually normalised over the next five days. After a brief period of normality, counts increased. The diagnosis of spinal infection coincided with the peak TLC for eight patients. All these patients had neurological deficits. Two patients were diagnosed with spinal infection before the onset of neurological deficits. Their TLC at the time of diagnosis were normal. The same trend was observed in their Absolute neutrophil count. Apart from the above risk factors all of the patients had history of intravenous cannulation and nine of ten patients had Foley's catheterization during DF.

All patients had been managed with analgesics for their back pain following DF. Orthopaedic opinion was sought for persistent backache in only two of these patients, who on further evaluation were found to have spinal infection. All other patients had neurological deficits on first visit. Diagnosis had been delayed as backache and fever is also consistent with DF.

Diagnosis of spinal infection was established based on the clinical picture, inflammatory markers, radiological evaluation and pus culture. Of the eight patients with neurological deficits six underwent emergency surgical decompression. One patient was not fit for anaesthesia and other patient was not willing for surgical procedure. Both these patients were treated with parenteral antibiotics based on their blood culture and sensitivity reports. Of the two patients without neurological deficit- one patient had L2 - 3 discitis with spondylolisthesis and another patient had D12-L1 discitis and severe instability clinically. Both underwent surgical debridement and instrumented fusion.

Intra operative cultures were positive for MRSA in six patients, MSSA in one patient and Ps. aeruginosa in one patient. All of them received culture specific antibiotics for six weeks. We followed up the patient every two weeks with total count and inflammatory markers. Post-operative radiographs were taken immediately and at six weeks. We take advanced imaging like CT and MRI taken only in cases with persistent symptoms or complications. Surgically managed cases showed good neurological recovery with negative blood cultures and normal neutrophil count at six weeks review. We lost follow up of one patient who was not willing for surgical management. Another patient under medical treatment, who was not fit for surgical procedure had improvement in term of spinal symptoms. We did not encounter any early complications in the present study. One patient had pain during the latest follow up (6months) and on evaluation she was found to have worsening of L2-3 listhesis and lumbar canal stenosis (Figure 1 to 8).

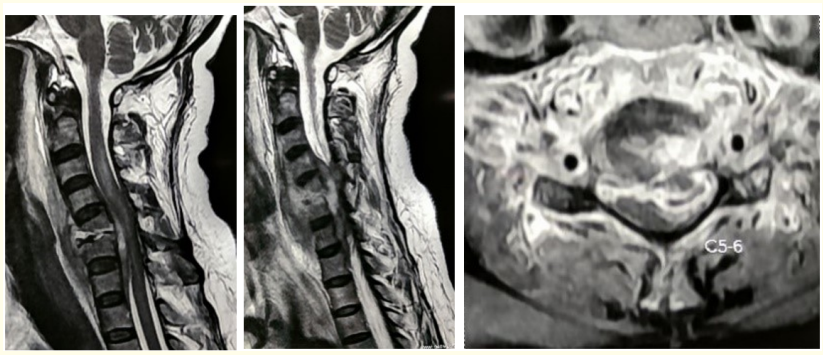


Figure 1 (a, b, c)

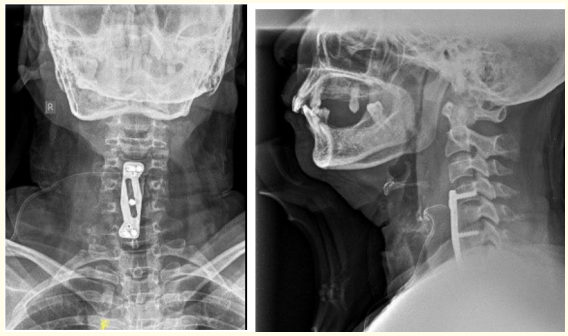
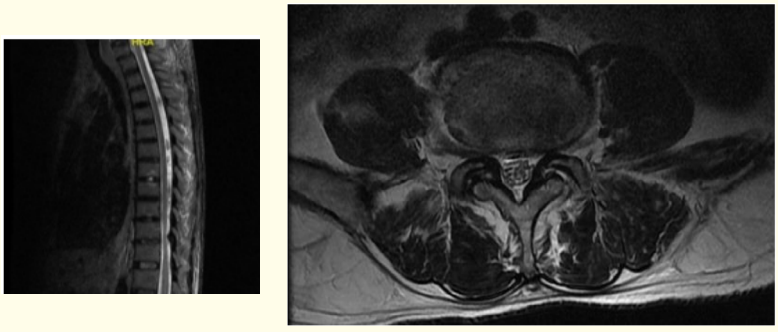


Figure 2 (a, b)



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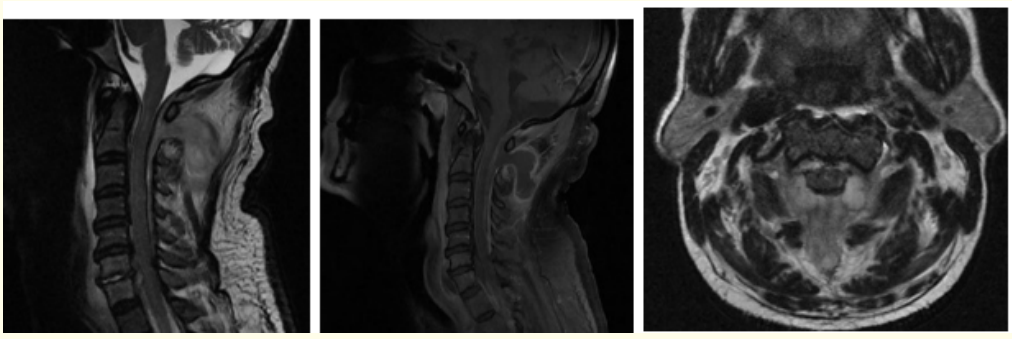

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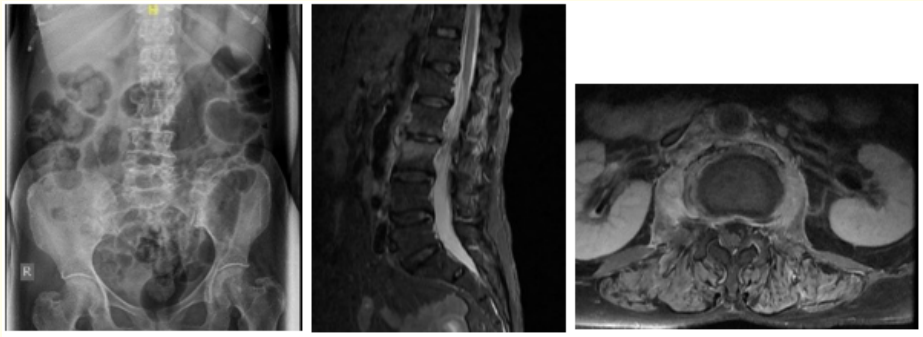


Figure 5 (a, b, c)

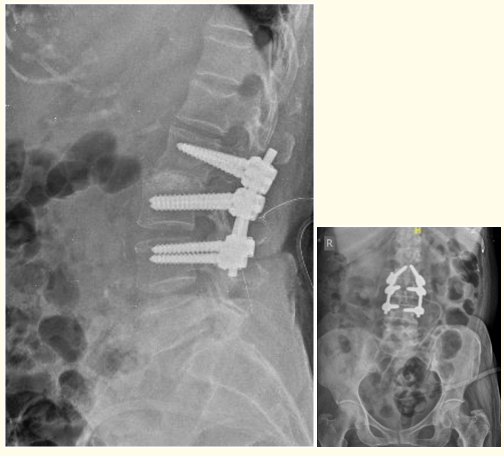


Figure 6 (a, b)

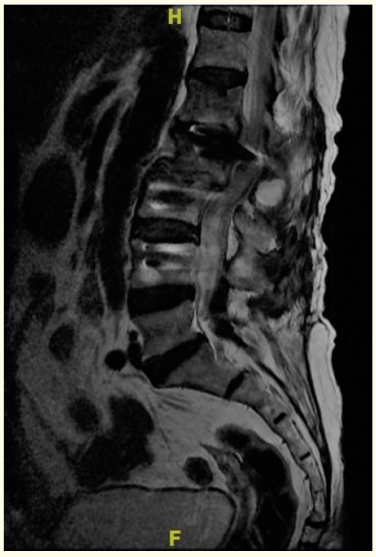


Figure 7

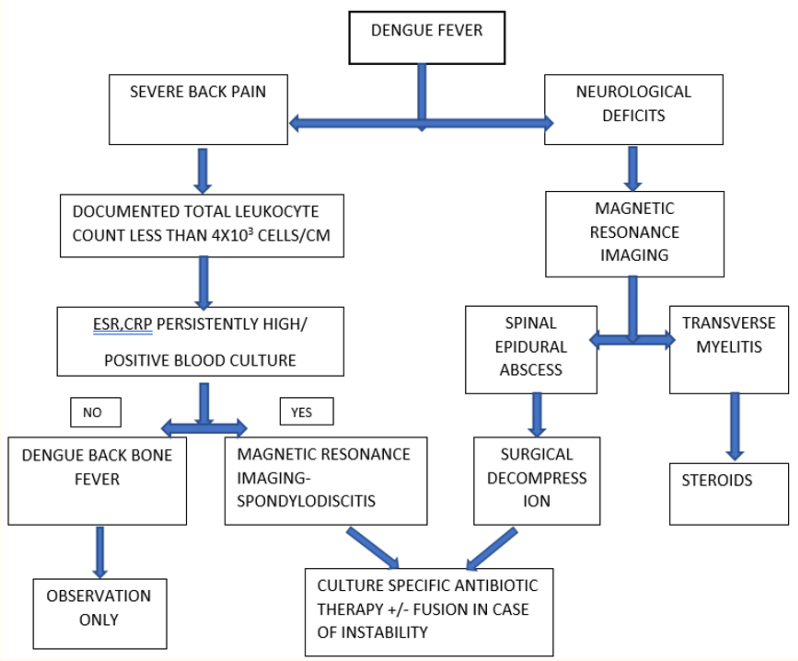
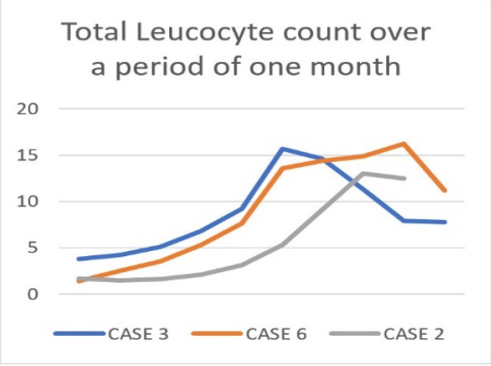


Figure 8: *Algorithm proposed by us to prevent delay in diagnosing spinal infections in DF.*

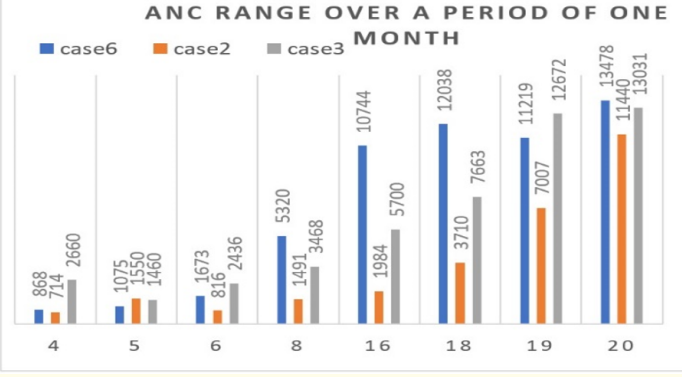
Apart from Type 2 DM there were no other pre-existing risk factors pertaining to the pyogenic spondylodiscitis. Back ache was the most common symptom. Those patients with persistent pain progressed to weakness due to epidural abscess. In most of the cases back pain was considered as a part of dengue myalgia and ignored by the physicians. High grade fever, elevated inflammatory markers at the time of presentation with a documented history of Dengue related transient leukopenia, neutropenia and bacteraemia were observed universally. There was no outbreak of community acquired MRSA infection during this period in our institution.

Discussion

Pyogenic spinal infections are relatively uncommon and are particularly challenging to diagnose for the physicians on initial interaction. Literature reports a delay in diagnosis of up to two to six months for pyogenic spinal infections and 75% of them being missed at initial physician interaction [3]. Doutchi., *et al* reported a mean time to diagnosis of 36 days, signifying the delay in diagnosis [4]. In the meantime, infection would progress to epidural abscess, vertebral body fracture or psoas abscess. They can present with varying degrees of neurological involvement in delayed presentations with poor outcome. Delay in diagnosis is also much more common in DF as the predominant symptoms, back pain along with myalgia may be considered as the prodrome (Graph 1 and 2).



Graph 1: *Range of total leucocyte count over a month.*



Graph 2: *Range of Absolute neutrophil count over a month.*

Some of the described risk factors in the literature are Diabetes mellitus, Intravenous drug use, alcohol abuse, immunocompromised state, degenerative joint, surgery, spinal catheters, skin and soft tissue infections, Urinary tract infection, sepsis, chronic liver or kidney disease, acupuncture, nerve block etc [5-8]. Oncological history and rheumatological diseases have also been reported as risk factors [9]. M Vakili., *et al.* in their series of 101 cases encountered various risk factors and 85% of them were diabetes mellitus and intravenous drug abuse [10]. Chu A., *et al* reported similar results [11]. Kumar A in their review reported that even normoglycemic patients are at high risk of spinal infections [12]. All our cases were secondary to hematogenous spread from the bacteraemia. Diabetes mellitus was present in 5 of our patients. Though all our patients had catherization the causative organisms were MRSA in most of the cases in contrast to the study by Pigrau C., *et al* [13], where CONS was the causative organism.

A "meta-analysis" reported several risk factors like psoas abscess, vaginal infection, and typhus as sources of infection. This is mainly based on several smaller case series and case reports. Psoas abscess can be a complication of spinal infection or a bowel infection [6].

Dengue as a risk factor hasn't been described in any of the studies in literature. We have had ten patients with spinal infections during the DF epidemic. All these patients had significant leukopenia (count < 4 x 10^3 cells/cm) and varying degrees of neutropenia. They have had hospital admissions and intravenous antibiotics for bacteraemia. Most of the patients are above 50 years and 50% are diabetic. Only possible explanation could be dengue associated immunosuppression and concomitant intravenous catheterization leading to bacteraemia and sepsis. But the predilection for spine couldn't be ascertained in the present study. There was no incident of other musculoskeletal infection during this period in DF patients. There was a delay in diagnosis with an average of 14 days from the diagnosis of DF in our patients. This was significant because delay in diagnosis directly related to the degree of neurological compromise, either by an expanding epidural abscess or vertebral fracture. Alba Riberia et al proposed risk factors for vertebral fracture following osteomyelitis: osteopenia, delayed diagnosis and dorsal spine involvement[14].

Medical management of these spinal infections has high failure rate as reported by Stratton in a meta-analysis, surgical decompression and fusion at earlier stage can aid in the neurological recovery of these patients [15]. Talia AJ reported Debridement and fusion at a single stage provides stability and eradicating the focus of infection. They have significant impact on reducing pain, aiding neurological recovery and ambulation, quality of life [16]. Park KH reported similar results. Current treatment protocols with prompt early diagnosis and appropriate medical and surgical managements have improved clinical outcome in vertebral osteomyelitis and spinal epidural abscess [17].

In a study by Thein TL., *et al* 2014 [2], neutropenia in dengue patients were reviewed. They found that severe neutropenia is prevalent in 11.8% of cases and ANC was lowest on 5th days. They also concluded that severe neutropenia was not predictive of a more serious disease and was not associated with secondary bacterial infection. In our brief review of PubMed database, a correlation between dengue related immunosuppression and spinal infections have not been documented. But in our series of ten cases, we observed a definite relation between leukopenia, neutropenia and spinal infections.

In expanded syndrome definition by WHO sepsis is considered a component. We would like to hypothesize that owing to an increased risk of spinal infections secondary to dengue related immune suppression and sepsis, the inclusion of spinal infections in expanded dengue syndrome might increase awareness among the physicians, facilitate early diagnosis and appropriate management. And it will reduce the unwanted delays in diagnosis, as even dengue fever can result in severe back ache. The following algorithm is proposed by us for DF patients to differentiate back ache due to infection and other causes.

Conclusion

A large-scale case control study is needed to prove the correlation between DF related leukopenia and spinal infections. But the pattern we observed at our institution during the dengue epidemic cannot be dismissed. Even though some of the observed patients had other risk factors for spine infection, all of them consistently had expanded dengue syndrome (DF, neutropenia and bacteraemia). With the

proposed algorithm we expect to diagnose the condition earlier. We would also like to conclude that including spinal infections as a part of expanded dengue syndrome might create more awareness among the physicians thereby aiding in early diagnosis and management.

We have no conflicts of interest or financial supports to disclose.

We certify that we have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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